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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/030,606	02/25/98	XU J	210121.428C3

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EXAMINER	
EYLER, Y	

ART UNIT	PAPER NUMBER
1642	10

DATE MAILED: 12/06/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary	Application No. 09/030,606	Applicant(s) Xu et al.
	Examiner Yvonne Eyler	Group Art Unit 1642

☒ Responsive to communication(s) filed on *Sep 13, 1999*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *8 and 9* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *8 and 9* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *5,6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

— SEE OFFICE ACTION ON THE FOLLOWING PAGES —

DETAILED ACTION

1. Applicant's election without traverse of Group IV, claims 8 and 9 and species of SEQ ID NOS. 110, 111, 115, 172-175, 177, 223 and 224 in Paper No. 9 is acknowledged.

Claims 1-7 and 10-22 have been canceled by amendment. Claims 8 and 9 are under consideration in the application.

Specification

The disclosure is objected to because of the following informalities:

The first line of the specification contains a blank which should be replaced with the application serial number from which this case depends. The continuing data should also be updated to indicate that U.S. serial number 08/806596 is now abandoned.

Page 3 of the specification refers to attached drawings, but there are no drawings.

Appropriate correction is required.

Claim Rejections - 35 USC § 112

2. Claims 8 and 9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

The recitation of an "immunogenic portion" is vague and indefinite because the metes and bounds of the specified portion cannot be determined. The specification teaches on page 4 that an

immunogenic portion of a prostate protein is any portion of any size that elicits an immune response in a patient inflicted with prostate cancer. There is no limitation or teaching, however, regarding definitive characteristics of the "portion" claimed and any portion would be expected to raise an immune response which is not unequivocally definitive of the instant proteins and nucleic acids encompassed.

Similarly, the recitation of "variants thereof" is also vague and indefinite because the metes and bounds of the encompassed proteins and therefore the encompassed nucleic acids cannot be determined. The specification on page 4 discloses that a variant includes any modification in which therapeutic, antigenic, or immunogenic properties are retained. There is no definition of these properties in such a way to definitely identify the encompassed proteins and encoding nucleic acids.

SEQ ID NO: 172 is an amino acid sequence not a nucleic acid sequence as claimed.

3. Claims 8 and 9 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for detecting nucleic acids comprising SEQ ID NOS: 110, 111, 115, 173-177, 223 or 224, does not reasonably provide enablement for detection of prostate cancer. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to practice the invention commensurate in scope with these claims.

The factors to be considered have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working

examples, the nature of the invention, the state of the prior art, the relative skill of those in the art, the predictability or unpredictability of the art and the breadth of the claims. *Ex Parte Forman,* (230 USPQ 546 (Bd Pat. App. & Int. 1986)); *In re Wands,* 858 F.2d 731, 8 USPQ 2d 1400 (Fed. Cir. 1988).

The instant specification provides insufficient evidence, no working examples, insufficient guidance and no indication from the prior art that it is predictable that the disclosed nucleic acid sequences are diagnostic of prostate cancer. Elevated levels of mRNA comprising SEQ ID NOS: 110, 111, 223, and 224 were detected in both tumorous and normal prostatic tissue, and no further information is provided to render it predictive that presence of these sequences is correlative with prostate cancer. The mere presence of mRNA within prostatic tissue-both normal and tumorous, absent objective evidence to the contrary, is not correlative with prostate cancer. While the sequences disclosed may be expressed to higher levels in prostatic tissue and therefore indicative of cells of prostate origin, there is no objective evidence that the mere detection of sequences which amplify using oligonucleotides specific for SEQ ID NOS: 110, 111, 115, 173-175, 177, 223, and 224 would enable one of skill in the art to detect prostate cancer.

Further, the claims encompass the detection of DNAs that encode protein products of genes from which the cDNA clones of the instant application were derived and also of DNAs with little to no relation to the instantly disclosed sequences.

The instant specification discloses the cloning and sequencing of cDNA segments from subtraction of expression libraries. No other DNA molecules are disclosed nor is objective evidence provided regarding the encoded polypeptide, immunogenic portions thereof, or variants. There is no description or working example of definitive identifying characteristics of the encoded polypeptides, i.e. molecular weight, shape, membrane association or other cellular location, pI, defining biological activity or function or even assays which reliably and predictably detect the polypeptides or of the full length cDNA which encodes the polypeptides. Further, there is insufficient objective evidence that the cDNAs that correspond to the SEQ ID NOS mentioned in the claims are full-length and encode a polypeptide. Thus, the specification does not provide sufficient guidance to enable one of skill to isolate and identify the full scope of claimed DNAs. See *Amgen Inc. v. Chugai Pharmaceutical Co.,* 927 F.2d. 1200, 18 USPQ2d 1601 (Fed. Cir. 1991); *Fiers v. Revel,* 984 F.2d 1164, 25 USPQ2d 1601 (fed. Cir. 1993); and *University of California v. Eli Lilly,* 119 F.3d 1559, 43 USPQ2d 1398 (Fed. Cir. 1997).

Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify the full scope of the DNA claimed. For reasons outlined below, one of skill in the art would be compelled to perform undue experimentation to obtain the complete gene that corresponds to any given partial-length cDNA such as those disclosed in the instant application and mentioned in the instant claims.

The instant application fails to provide an enabling disclosure for sequences additional to the specific sequences disclosed and therefore, for there detection. While recombinant cloning

techniques have been known since the discovery of restriction enzymes in 1974, such cloning techniques may present difficulties which need to be addressed for each gene under consideration. In many cases, the cloning of a gene involves consideration of such factors as complex gene structures, presence of repetitive gene sequences, and presence of closely related genes that cross hybridize with one another. To clone cDNAs, consideration of one or both of the following are important:

(a) the presence of alternatively spliced variants of primary gene transcripts and

(b) physical difficulties in preparing full-length cDNA molecules due to the presence of significant mRNA secondary structure which can result in artifacts of reverse transcription.

Several specific examples from more recent literature illustrate problems related to the cloning of genes and cDNA transcripts even in cases where a particular nucleic acid probe was available. In the case of the cloning of the gene for polycystic kidney disease, difficulties were encountered because of the complex structure of the locus and the presence of cross-hybridizing genetic elements. (Harris et al. J. of the Am Society of Nephrology 6:1125-33, 1995).

In the case of the dystrophin gene, even more problems were encountered (Ahn et al. Nature Genetics 3(4):283-91, 1993). Expression of this gene is under elaborate transcriptional and splicing control. At least five independent promoters specify the transcription of their respective alternative first exons in a cell-specific and developmentally controlled manner. Three promoters express full-length dystrophin, while two promoters near the C-terminus express the

last domains in a mutually exclusive manner. Six exons of the C terminus are alternatively spliced, giving rise to several alternative forms.

A final example of the complications that may be encountered when cloning genes is the discovery of genes within genes (Cawthon et al. Genomics 9(3):446-60, 1991).

Thus, one of skill in the art, armed with any one of the EST sequences and the guidance in the instant application, would not have been able to obtain a cloned genomic gene corresponding to or related by any particular level of sequence identity to any particular EST without undue experimentation.

Given the undue experimentation required to make and or use the full scope of the claimed DNAs, it would also require undue experimentation to detect DNAs encoding variants or immunogenic portions of polypeptides. Additionally, there is no description or guidance regarding the regions of the polypeptides which are definitive of specific antigenic regions or which are required to maintain identifying characteristics, it would require undue experimentation to identify variants or immunogenic portions, even if the polypeptides were enabled. There is no guidance regarding which portions of the polypeptide are immunogenic and definitive nor is there guidance regarding which regions of the polypeptide may be deleted, substituted etc. while still maintaining the activity of the polypeptide. Since detailed information regarding the structural, functional, and immunogenic requirements and properties of the polypeptide are lacking, it is unpredictable as to which amino acid substitutions, if any, meet the limitations of the claim. Furthermore, while recombinant techniques are available, it is <u>not</u> routine in the art to screen large

numbers of substituted proteins where the expectation of obtaining similar activity is unpredictable based on the instant disclosure.

Thus, given the undue amount of experimentation required to identify the extensive nucleic acid sequences encompassed, it would require undue experimentation to amplify and identify these sequences and further, it would require undue experimentation to detect prostate cancer using any disclosed sequence as detailed above.

Claim Rejections - 35 USC § 102

4. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

5. Claims 8 and 9 are rejected under 35 U.S.C. 102(e) as being anticipated by Bandman et al. (U.S. No. 5, 786,148-IDS).

Bandman et al. teach a DNA encoding a human prostate-specific kallikrein (HPSK). Bandman et al. further teach the detection of the presence of polynucleotide sequences encoding HPSK using oligonucleotides of at least about 10 nucleotides by either hybridization or PCR protocols and teach such detection to be useful for diagnosis of conditions or diseases which are

associated with HPSK expression including prostate cancer. See the abstract; column 14, lines 46-57; and column 22.

The nucleic acids and methods of diagnosis taught by Bandman et al. meet the limitations encompassed by the instant claims. The nucleic acids of Bandman et al. encode an immunogenic portion or variant of the polypeptides encoded by a DNA comprising SEQ ID NOS 173-177, see the attached results of sequence comparisons.

NO CLAIM IS ALLOWED.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Yvonne Eyler, Ph.D. whose telephone number is (703) 308-6564. The examiner can normally be reached on Monday through Friday from 830am to 630pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Paula Hutzell, can be reached on (703) 308-4310. The fax phone number for this Group is (703) 305-3014 or (703) 308-4242.

Communications via Internet e-mail regarding this application, other than those under 35 U.S.C. 132 or which otherwise require a signature, may be used by the applicant and should be addressed to [**paula.hutzell@uspto.gov**].

All Internet e-mail communications will be made of record in the application file. PTO employees do not engage in Internet communications where there exists a possibility that sensitive information could be identified or exchanged unless the record includes a properly signed express waiver of the confidentiality requirements of 35 U.S.C. 122. This is more clearly set forth in the Interim Internet Usage Policy published in the Official Gazette of the Patent and Trademark on February 25, 1997 at 1195 OG 89.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Yvonne Eyler

Yvonne Eyler, Ph.D.
Primary Examiner
December 5, 1999